

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

REC'D 03 MAR 2005



WIPO PCT

Applicant's or agent's file reference K 2851 PCT	FOR FURTHER ACTION See Form PCT/PEA/416	
International application No. PCT/US2004/010737	International filing date (day/month/year) 07.04.2004	Priority date (day/month/year) 07.04.2003
International Patent Classification (IPC) or national classification and IPC C07D213/79, C07D213/80, C07D401/12, C07D403/12, C07D413/12, C07D417/12, A61K31/423, A61K31/428, A61K31/454, A61K31/465, A61K31/502, A61K31/506, A61P3/00		
Applicant KALYPSYS, INC et al.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
 - a. ☐ sent to the applicant and to the International Bureau) a total of sheets, as follows:
 - ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
 - ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
 - b. ☐ (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

Date of submission of the demand 08.11.2004	Date of completion of this report 01.03.2005
Name and mailing address of the International preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Hanisch, I Telephone No. +49 89 2399-7880 

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
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Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This report is based on translations from the original language into the following language, which is the language of a translation furnished for the purposes of:
 - ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-94 as originally filed

Claims, Numbers

1-124 as originally filed

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
 - ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):
 4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
 - ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:
- ☐ the entire international application,
 - ☒ claims Nos. 1,29-32,59-62,92-95 (all part),97-119
because:
 - ☒ the said international application, or the said claims Nos. 97-119 with respect to industrial applicability relate to the following subject matter which does not require an international preliminary examination (specify):
see separate sheet
 - ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
 - ☒ the claims, or said claims Nos. 1,29-32,59-62,92-95 (all part) are so inadequately supported by the description that no meaningful opinion could be formed.
 - ☐ no international search report has been established for the said claims Nos.
 - ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
 - ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
 - ☐ See separate sheet for further details

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	2-96,100-115,121-124
	No: Claims	1,97-99,116-120
Inventive step (IS)	Yes: Claims	
	No: Claims	1-124
Industrial applicability (IA)	Yes: Claims	1-96,120-124
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

**INTERNATIONAL PRELIMINARY
REPORT ON PATENTABILITY
(SEPARATE SHEET)**

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Re Item III.

Claims 97-119 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Moreover, it is noted that the application refers to "prodrugs" and "metabolites". These terms are functional definitions which attempt to define a chemical compound in terms of a result to be achieved without giving a specific technical guidance for the selection of the suitable derivatives in the description and without proven general knowledge to show which derivatives in this specific case are suitable prodrugs. The term could be seen as a mere invitation to the skilled person to perform a research program in order to find the suitable variants. In such a situation, when the invention cannot be carried out over the whole claimed area without imposing an undue burden on the skilled person, the disclosure may be considered insufficient, even when simple in vivo or in vitro tests are available to determine whether or not a particular compound is covered by the claims. Therefore, the said terms have not been searched and do not part form part of the examined current subject-matter.

Re Item V.

The following documents are referred to in this communication:

- (A) J. Med. Chem. 1971, vol. 14, no. 4, pages 369-370
- (B) US 4206117 A
- (C) WO 0230895 A
- (D) WO 0064888 A
- (E) EP 1067109 A
- (F) WO 9728149 A

Novelty

The current general formula I appears not to be novel in the sense of Article 33(2) PCT since (A)-(C) disclose specific compounds falling within its scope. However, the current part overlapping with (D) appears to be a novel selection of (D) and the current compounds essentially differ from those of (E) and (F) on account of the O-(CH₂)₃-N-linker.

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Inventive Step

The problem underlying the current application is considered to be the provision of further PPAR-modulators which are useful for the treatment of e.g. atherosclerosis. (C) appears to be the closest prior art disclosing compounds which fall within the current general formula and have the desired activity. An inventive step could therefore only be acknowledged for a delimited subject-matter with an improved effect which in the light of the closest prior art is surprising. Such an unexpected effect appears not to be present in the application documents so that the current subject-matter at present does not satisfy Article 33(3) PCT.

Industrial Applicability

For the assessment of the present claims 97-119 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Items VII. and VIII.

It is noted that claim 95 appears not to be clear in the sense of Article 6 PCT since "KP001" etc. are no generally known definitions or names and, moreover, the description does not unambiguously assign specific compounds to these expressions: The headings in table 1 (pp 22-30) are unreadable but apparently lack the definition of 3 substituents, and the following pages define one substituent without specifying the other 2-3 missing substituents. Concerning the opinion given above it is preliminarily assumed that claim 95 in fact is a dependant claim of claim 1.

Box No. VIII (iv) DECLARATION: INVENTORSHIP (only for the purposes of the designation of the United States of America)
The declaration must conform to the following standardized wording provided for in Section 214; see Notes to Boxes Nos. VIII, VIII (i) to (iv) (in general) and the specific Notes to Box No. VIII (iv). If this Box is not used, this sheet should not be included in the request.

**Declaration of inventorship (Rules 4.17(iv) and 51bis.1(a)(iv))
 for the purposes of the designation of the United States of America:**

I hereby declare that I believe I am the original, first and sole (if only one inventor is listed below) or joint (if more than one inventor is listed below) inventor of the subject matter which is claimed and for which a patent is sought.

This declaration is directed to the international application of which it forms a part (if filing declaration with application).

This declaration is directed to international application No. PCT/..... (if furnishing declaration pursuant to Rule 26ter).

I hereby declare that my residence, mailing address, and citizenship are as stated next to my name.

I hereby state that I have reviewed and understand the contents of the above-identified international application, including the claims of said application. I have identified in the request of said application, in compliance with PCT Rule 4.10, any claim to foreign priority, and I have identified below, under the heading "Prior Applications," by application number, country or Member of the World Trade Organization, day, month and year of filing, any application for a patent or inventor's certificate filed in a country other than the United States of America, including any PCT international application designating at least one country other than the United States of America, having a filing date before that of the application on which foreign priority is claimed.

Prior Applications:

I hereby acknowledge the duty to disclose information that is known by me to be material to patentability as defined by 37 C.F.R. § 1.56, including for continuation-in-part applications, material information which became available between the filing date of the prior application and the PCT international filing date of the continuation-in-part application.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Name: Kevin LIU

Residence: San Diego, California

(city and either US state, if applicable, or country)

Mailing Address:

Citizenship: UNITED STATES OF AMERICA

Inventor's Signature: Kevin Liu
 (if not contained in the request, or if declaration is corrected or added under Rule 26ter after the filing of the international application. The signature must be that of the inventor, not that of the agent)

Date: 4/22/2004
 (of signature which is not contained in the request, or of the declaration that is corrected or added under Rule 26ter after the filing of the international application)

Name: Cunxiang ZHAO

Residence: San Diego, California

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Mailing Address: 4178 Decoro Street #18, San Diego, California 92122, UNITED STATES OF AMERICA

Citizenship: P.R. CHINA

Inventor's Signature: Cunxiang Zhao
 (if not contained in the request, or if declaration is corrected or added under Rule 26ter after the filing of the international application. The signature must be that of the inventor, not that of the agent)

Date: 4/23/2004
 (of signature which is not contained in the request, or of the declaration that is corrected or added under Rule 26ter after the filing of the international application)

☐ This declaration is continued on the following sheet, "Continuation of Box No. VIII (iv)".